UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/732,669	12/08/2000	Todd A. Blumenkopf	PC10609ABTC	2857

7590 04/19/2002

Gregg C. Benson
Pfizer Inc.
Patent Department MS 4159
Eastern Point Road
Groton, CT 06340

EXAMINER
BALASUBRAMANIAN, VENKATARAMAN

ART UNIT	PAPER NUMBER
1624	8

DATE MAILED: 04/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/732,669	BLUMENKOPF ET AL.	
	Examiner	Art Unit	
	Venkataraman Balasubramanian	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4 & 5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election with traverse of Group I, claims 1-20 in Paper No. 7, is acknowledged. Claims 21-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group II. However, upon further consideration, in view of applicants' traversal and prior art search, the restriction requirement is withdrawn and claims 1-26 will be examined as a whole.

Claims 1-26 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following reasons apply. Any claim not specifically rejected is rejected as being dependent on a rejected claim.

1. Claim 1 is indefinite as the definition of R^5 is unclear. Note in line 20 of claim 1, R^5 is recited as $(C^1\text{-}C^6)$alkylamino, amino $(C^1\text{-}C^6)$alkyl but again in line 23 it recites the same groups. It is not clear what is the difference between these two definition of R5 .The definition of R^5 is therefore ambiguous.
2. Recitation of the term " alkyl" in claim 1 is indefinite as specification on page 5 offers two distinct definitions for the same term. The term " alkyl" is defined on page 5, line 12-14 differs from that is recited in lines 22-27 which not only include cyclic alkyl with examples as several cycloalkyls but also halogen substituents. It

is not clear what is difference between "alkyl" and "cycloalkyl" recited in the claims. Similarly, it is unclear what is "haloalkyl" defined in claim 1 and the alkyl with halogen substituents recited in specification.

3. Claims 21,22, 24 and 26 are indefinite as these claims recite the broad recitation "cancer", and the claim also recites "leukemia" which is the narrower statement of the range/limitation. Note this a double inclusion of single element leukemia in a broader limitation "cancer". See also Ex parte White 127 USPQ 261.

In addition these claims recite "other autoimmune diseases" which is unclear as to what these "other autoimmune diseases" are. Specification has no definition of this term.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating psoriasis, does not reasonably provide enablement for treating or preventing all diseases embraced in the instant invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Method claims 23-26 and pharmaceutical composition claims 21-22 with intended uses are not adequately enabled for the range of diseases recited therein.

From the reading of specification, it appears that the applicants are asserting that the embraced compounds because of their mode action, which involves inhibition of Janus family of tyrosine kinase(s), would be useful for all sorts of diseases including autoimmune diseases, cancer, Alzheimer's disease, various arthritis, multiple sclerosis etc. However, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended mammal. Moreover many if not most of diseases such as rheumatoid arthritis, sepsis, chronic hepatitis, multiple sclerosis, Alzheimer's disease etc. are very difficult to treat and hardly possible to prevent as claimed herein. For multiple sclerosis alone there is no known drug, which can successfully reverse the course of the disease, despite the fact that there are many drugs, which can be used for "inflammatory condition". Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288 . Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

The instant claims are drawn to 'a method for treating or preventing a disorder or condition selected from organ transplant rejection, lupus multiple sclerosis rheumatoid arthritis etc. The scope of the claims includes not only treatment but also "prevention of a disease" which is not adequately enabled solely based on the activity of the compounds as tyrosine kinase or Janus kinase 3 inhibitors provided in the specification at pages 25-26. "To prevent" actually means to anticipate or counter in advance, to

keep from happening etc. (as per Websters II Dictionary) and there is no disclosure as to how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "prevention" effect. There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein. Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed 'preventive' effect solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See Traxler (provided).

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating or preventing all diseases due to tyrosine kinase inhibitory activity.

2) The state of the prior art: Although there are several tyrosine kinase inhibitors known, they have not prevented or able to treat all diseases embraced in the

instant claims. 3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for the 'preventive' effect of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: There is no supporting evidence that all diseases embraced are treatable and even preventable in view of their tyrosine kinase activity.

6) The breadth of the claims: The instant claims embrace not only treatment but also the prevention of diseases.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of

the claimed compounds towards 'preventing' the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-26 rejected under 35 U.S.C. 103(a) as being unpatentable over Cockerill et al. WO 98 02438.

Cockerill et al. teaches bicyclic heteroaromatic compounds, which include compounds claimed herein, as protein tyrosine kinase inhibitors for the treatment of psoriasis. See page 7, formula I and note the definition of X, A, Y, U, R', R^1, R^2 p and n.

On pages 7-10, note when X is N and A is choice 8, Y is W-CH_2 or W and W is NR_a where R_a is C_7-C_8 alkyl and U is mono or bicyclic ring system, the compounds taught by the reference include generically those claimed herein. Note instant proviso is not applicable due to Ra and Y definition. See pages 11-24 for various preferred embodiments. See the process of making shown on page 24-25. See also examples 1-41 on pages 49-61 for experimental details for making these class of compounds.

Claims rejected herein require a pyrrolopyrimidine core. However Cockerill et al. teaches the equivalency of exemplified core and the substituents shown in examples 1-41 with those contemplated and claimed in the definition of various groups of formula I. See page 7, formula I and note the definition of X, A, Y, U , R', R1 , R2 , p and n. Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds with pyrrolopyrimidine core variously substituted in said ring as permitted by the reference and expect resulting compounds (instant compounds) to possess the uses taught by the art in view of the equivalency teaching outline above

Claims 1-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buzzetti et al. EP 0 795 556.

Buzzetti et al. teaches several 4-substituted pyrrolopyrimidine compounds, which include compounds, claimed herein for the use as tyrosine kinase inhibitors for anti-cancer therapy. See formula I on page 2 and note the definition of X, A, R, R_1, R_2, R_3, R_4 and n. Note when X is $NH(CH_2)n$ where n=1 and A is pyridyl, oxindolyl, indolyl, quinolinyl and isoquinolinyl, the compounds taught by the reference is also embraced in

the instant claims when R_5 is $R_{14}(C_1\text{-}C_6)$alkyl) = $(C_2\text{-}C_9)$ heterocycloalkyl$(C_1\text{-}C_6)$alkyl). See page 3 for list of preferred compounds and process of making on page 4-6 and examples 1-6 on page 8-10.

Reference differs from the instant claims in not exemplifying pyrrolopyrimidine with 4-NH-CH_2-hetrocycloalkyl group. However Buzzetti et al. teaches the equivalency of exemplified 4-NH-hetrocycloalkyl group shown in examples 1-6 with those contemplated and claimed in the definition of various groups of formula I. See formula I on page 2 and note the definition of X, A, R, R_1, R_2, R_3, R_4 and n. Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds with pyrrolopyrimidine core variously substituted in said ring with including 4-NH-CH2-hetrocycloalkyl group as permitted by the reference and expect resulting compounds (instant compounds) to possess the uses taught by the art in view of the equivalency teaching outline above.

Claim Objections

Claims 22, 24 and 26 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims of 21, 23 and 25. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-26 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim1-12 of copending Application No. 09/956,645. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter embraced in the instant claims is also embraced in the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

References cited in the Information Disclosure Statements (paper # 4 & 5)are made of record.

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (703) 305-1674. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 5.30 PM.

The fax phone number for the organization where this application or proceeding is assigned (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

V. Balasubramanian
Venkataraman Balasubramanian

4/18/2002